

REMARKS

The Office Action dated December 27, 2007 has been carefully reviewed and the following remarks are made in response thereto. In view of the following remarks, Applicants respectfully request reconsideration of this application and timely allowance of the pending claims.

Status of the Claims

Claims 83, 84, 87, and 88 are pending in the present application.

Claim Rejections under 35 U.S.C. § 103(a)

Claims 83, 84, 87, and 88 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent No. 6,113,907 to Khwaja et al. ("Khwaja et al.") in view of U.S. Patent No. 6,040,138 to Lockhart et al. ("Lockhart et al."). Specifically, the Examiner asserts that Khwaja et al. disclose the use of certain bioassays, but not genomic based bioassays, for ensuring quality of a botanical product, while Lockhart et al. describes a method of using gene array, i.e., a genomic based bioassays, for monitoring the expression levels of multiple pre-selected genes. Thus, the Examiner alleges that it would have been obvious to one skilled in the art to combine the gene array method of Lockhart et al. with the quality control method of Khwaja et al. to arrived at the present invention.

Applicants respectfully submit that the cited references in combination do not render the claimed invention obvious for the reasons discussed as follows.

Establishing *prima facie* obviousness requires a showing that the prior art references, when combined, teach or suggest all the claim limitations. Furthermore, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Recently, the United States Supreme Court also expressed the need to an "explicit" showing of "some apparent reason to combine the known elements in the fashion claimed by the patent at issue" and that "rejection on obviousness grounds cannot be sustained by mere

conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, slip op. at 14 (2007).

First, Applicants respectfully submit that the combined disclosures of the cited references do not disclose or suggest all the claim limitations of the present method.

Khwaja et al. disclose a method for standardizing St. John's Wort from various sources and/or in various forms so that they may be used more effectively in treating certain diseases. As the Examiner acknowledges, the Khwaja method does not use genomic based bioassays, as the present method does. More importantly, while the Khwaja method is based on measuring series of biological activities of the individual fractions of St. John's Wort extract, the claimed method is based on measuring the biological response of a biosystem when the biosystem is exposed to a whole batch, not fractions, of a herbal composition. More specifically, the Khwaja method comprises the step of separating the botanical composition into a plurality of marker fractions and determining the biological activity of each of the marker fractions to provide a bioactivity fingerprint (col. 9, lines 9-14; col. 9, lines 24-30; col. 9, lines 56-62; and Fig. 6). In contrast, steps (b)(i) and (c)(i) of the present method indicate that the biosystem is exposed to a whole batch of a herbal composition, either the standard batch or the test batch, not a fraction or fractions of any batch.

Lockhart et al. disclose a method of monitoring the expression levels of a multiplicity of pre-selected genes by using high density oligonucleotide arrays. Lockhart et al. also contemplate using the disclosed gene array method for monitoring genes associated with certain pathological conditions or genes involved in particular biological pathways (column 4, line 64 to column 5, line 12). However, Lockhart et al. do not disclose or even remotely suggest using the disclosed method for quality control of herbal compositions, let alone the steps of exposing whole batches of herbal compositions to a biosystem.

Thus, the combined disclosures of Khwaja et al. and Lockhart et al. fail to disclose all the claim limitations of the present method, which include, *inter alia*, exposing a whole batch of herbal composition and determining its differential gene expression profile via a genomic-based assay method.

Furthermore, there is no suggestion available in the cited references or otherwise of the record which would motivate one skilled in the art to combine the method disclosed in each of the cited references and further modify it in such a way to arrive at the present invention.

It is true that both Khwaja et al. and the present invention have the similar general objectives of resolving the quality control problem in botanical or herbal compositions, but Khwaja et al. and the present invention are directed to fundamentally different ways to achieve their goals. As noted above, Khwaja et al. uses fractionation approach, while the present invention uses the whole herbal extract. Furthermore, the bioassays in Khwaja et al. involve measuring the activity of a single enzyme or protein receptor known to be associated with a specific disease to assess the biological efficacy of a compound or substance in treating the disease. In contrast, the present method involves, *inter alia*, measuring the gene expression levels of multiple genes which may or may not have any relationship to any diseases or particular biological pathways but still monitoring batch to batch equivalency.

Although Lockhart et al. disclose a gene array method, Lockhart et al. teach away from the present invention. Lockhart et al. involves the typical use of gene arrays, which is focused on discovery of underlying biological mechanisms of diseases. Specifically, Lockhart et al. suggest using the method for monitoring genes associated with certain biological specificities, such as specific diseases or biological pathways. For example, Lockhart et al. state:

"Genes of particular interest for expression monitoring include genes involved in the pathways associated with various pathological conditions (e.g., cancer) and whose expression is thus indicative of the pathological condition. Such genes include, but are not limited to the HER2 (c-erbB-2/neu) proto-oncogene in the case of breast cancer, receptor tyrosine kinases (RTKs) associated with the etiology of a number of tumors including carcinomas of the breast, liver, bladder, pancreas, as well as glioblastomas, sarcomas and squamous carcinomas, and tumor suppressor genes such as the P53 gene and other "marker" genes such as RAS, MSH2, MLH1 and BRCA1. Other genes of particular interest for expression monitoring are genes involved in the immune response (e.g., interleukin genes), as well as genes involved in cell adhesion (e.g., the integrins or selectins) and signal transduction (e.g., tyrosine kinases), etc." (column 4, line 64 to column 5, line 12; underline added)

In contrast, the present invention involves using a living cell as a detector to integrate the complex effects of a mixture of compounds in a whole batch of a herbal composition and read-out a differential genomic expression pattern for the purpose of quality control. Thus, unlike the

present method wherein the multiple genes, of which the gene expression levels are measured, may or may not have any relationship to any diseases or particular biological pathways, Lockhart et al. suggest measuring gene expression levels of the genes that are associated with specific diseases or biological pathways.

Moreover, as noted above, Lockhart et al. do not remotely suggest using the gene array method for quality control of herbal compositions, let alone the steps of exposing whole batches of herbal compositions to a biosystem.

Therefore, in view of the teaching away of Lockhart et al. and the lack of specific suggestions for modifying the Khwaja method, one skilled in the art would not be motivated to combine the prior art methods and further make such specific changes thereto in such a fashion that the present quality control method can be obtained.

Therefore, Applicants respectfully submit that the claimed invention is not rendered obvious by the combined disclosure of the cited references.

Conclusion

In view of the foregoing remarks, Applicants respectfully request withdrawal of the outstanding rejection and early notice of allowance to that effect. Should the Examiner believe that a telephonic interview would expedite prosecution and allowance of this application, he is encouraged to contact the undersigned at his convenience.

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No.50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

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